

VERIFICATION OF TRANSLATION

I, the below named translator, hereby declare that:

My name and post office address are as stated below:

That I am knowledgeable in the English language and in the language in which the below identified international application was filed, and that I believe the English translation of the international application No. PCT/JP2003/010820 is a true and complete translation of the above identified international application as filed.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date

February 8, 2005

Full name of the translator Ikuko AIHARA

Signature of the translator Ikuko Ahara

Post Office Address Kitahama TNK Building 7-1, Dosho-machi

1-chome, Chuo-ku, Osaka-shi, Osaka 541-0045,

Japan

- 1 -

#### DESCRIPTION

#### HAIR GROWTH STIMULANTS FOR ORAL USE

#### TECHNICAL FIELD

5 The present invention relates to a hair growth stimulant for oral use that exhibits excellent effects for hair loss prevention, hair regrowth, etc.

#### BACKGROUND ART

10 Recently, an increasing number of men and women are said to be suffering from thinning hair or hair loss caused by various changes in their social environment, such as an increase in stress factors and changes in eating habits, and thus the social expectations and needs  
15 for hair restorers have been increasing. Hitherto, hair restorers containing a variety of active ingredients that are intended to eliminate or alleviate the causes of thinning hair or hair loss have been developed. For example, hair restorers containing swertia herb extract or  
20 tocopherol acetate to increase the blood flow to the hair roots, or hinokitiol to improve scalp metabolism have been developed and used to prevent or treat alopecia.

It is believed, however, that various factors, such as hereditary factors, stress, eating habits and  
25 aging, are combined in a complicated manner to cause

thinning hair or hair loss. Thus, no satisfactory effects of hair loss prevention or hair regrowth can be obtained simply by adding swertia herb extract or other ingredients to improve blood flow or scalp metabolism, like hitherto known hair restorers.

5 Cat's whiskers (Orthosiphon aristatus (Blume) Miq.) and Orthosiphon stamineus Benth. are perennial plants of the genus Orthosiphon in the family Lamiaceae, and distributed across India, Southeast Asia, the northern 10 part of Australia, Okinawa in Japan, and elsewhere. In India, Malaysia and Indonesia, these plants are used as important folk medicines and known to have effects for alleviating the symptoms of acute or chronic nephritis, cystitis, urolithiasis, cholelithiasis, rheumatic 15 arthritis, diabetes and other diseases. Especially in Indonesia, these plants are called "kumis kuching" and are taken as effective folk medicines against nephritis, urolithiasis, etc.

Japanese Unexamined Patent Publication Nos. 20 1998-29924, 1999-228337, 2000-95663 and 2001-224330 reported use of plants of the genus Orthosiphon in the family Lamiaceae or extracts thereof as external medicines to be applied to the scalp, such as hair tonics or hair restorers. However, these medicines do not have 25 satisfactory effects.

Further, lilac chastetree (Vitex agnus-castus L.), simpleleaf chastetree (Vitex trifolia L.) and other plants are known as plants of the genus Vitex L. in the family Verbenaceae.

5           Lilac chastetree is distributed from Southern Europe to the western part of Asia. In Europe, its fruit is used as a flavoring or perfume and its leaves and fruit as medicines, such as a diuretic, a cold medicine, an aphrodisiac for males, an antidepressant for menopause, 10 etc. DE3442961 reported use of the plant body or an extract of lilac chastetree as a hair growth stimulant for external use, but with unsatisfactory effects.

Simpleleaf chastetree is widely distributed from the Korean Peninsula to Southeast Asia and Australia. In 15 China, the fruit of simpleleaf chastetree is called Man Jing Zi, and is used for the treatment of headaches and colds, alleviation of fever, pain relief, sedation, anti-inflammatory treatment, etc. The Chuyaku Jiten (Dictionary of Chinese Medicines; pp. 2456-2458) and 20 Japanese Unexamined Patent Publication Nos. 1984-116211 and 2000-31512 reported use of the plant body or an extract of simpleleaf chastetree as an external medicine to be applied to the scalp. However, the external medicine, such as a hair tonic or hair restorer, does not 25 exhibit satisfactory effects.

Use of plants of the genus Orthosiphon in the family Lamiaceae or the genus Vitex L. in the family Verbenaceae as a hair growth stimulant for oral use has not hitherto been known.

5

DISCLOSURE OF THE INVENTION

The main object of the present invention is to provide a hair growth stimulant for oral use that has excellent hair growth activity and significant effects for 10 hair loss prevention, hair regrowth promotion, etc.

The present inventors conducted extensive research to achieve the above object, and found that oral administration of a plant of the genus Orthosiphon in the family Lamiaceae or the genus Vitex L. in the family 15 Verbenaceae or an extract of the plant exhibits a higher hair growth effect than external use thereof. The inventors carried out further research and accomplished the present invention.

The present invention provides the following 20 hair growth stimulants for oral use and food for hair growth.

1. A hair growth stimulant for oral use comprising at least one member selected from the group 25 consisting of plants of the genus Orthosiphon in the

family Lamiaceae, plants of the genus Vitex L. in the family Verbenaceae, and extracts thereof.

2. The hair growth stimulant for oral use  
5 according to item 1, wherein the plants of the genus Orthosiphon in the family Lamiaceae are at least one member selected from the group consisting of cat's whiskers (Orthosiphon Aristatus (Blume) Miq.)),  
Orthosiphon grandiflorus Bold., Orthosiphon rubicundus  
10 Benth., Orthosiphon spicatus Benth., and Orthosiphon stamineus Benth.

3. The hair growth stimulant for oral use  
according to item 1, wherein the plants of the genus Vitex  
15 L. in the family Verbenaceae are at least one member selected from the group consisting of simpleleaf chastetree (Vitex trifolia L.), roundleaf chastetree (Vitex rotundifolia L.f.), hempleaf negundo chastetree (Vitex cannabifolia Sieb. et Zucc.), negundo chastetree  
20 (Vitex negundo L.), and lilac chastetree (Vitex agnus-castus L.).

4. The hair growth stimulant for oral use  
according to any one of items 1 to 3, which is a food for  
25 hair growth.

The present invention is described below in detail.

Plants of the genus Orthosiphon in the family Lamiaceae

5 Examples of plants of the genus Orthosiphon in the family Lamiaceae usable in the present invention include cat's whiskers (Orthosiphon aristatus (Blume) Miq.)), Orthosiphon grandiflorus Bold., Orthosiphon rubicundus Benth., Orthosiphon spicatus Benth.,  
10 Orthosiphon stamineus Benth., etc.

In the present invention, plants of the genus Orthosiphon in the family Lamiaceae may be used as ground products of raw or dried plants, or as extracts obtained by effectively extracting active ingredients from the  
15 plants.

The part of the plants to be used is not limited. The aboveground parts, such as stems, leaves and flowers, the subterranean parts, such as roots, or the whole plant can be used, with the aboveground parts being especially  
20 preferable.

Extracts of the plants can be obtained by chopping the raw or dried plant and subjecting the chopped plant to extraction with a suitable solvent, which is preferably water, a lower alcohol or a mixture thereof.

25 Lower alcohols usable for extraction include

$C_{1-3}$  alcohols, such as methanol, ethanol, etc., among which ethanol is most preferable. These alcohols may also be hydrous alcohol (water content: 0.1 to 99.9%).

The extraction can be performed by a batch 5 process, percolation process, reflux process or other known processes. The proportion of the extraction solvent is not limited, and is suitably 2 to 1000 parts relative to 1 part of the chopped raw or dried plant. The extraction can be carried out at room temperature or with 10 heating.

Preferably, the extraction is performed at a temperature range of room temperature to about 80°C for about 1 hour to about 10 hours while stirring under mild conditions. The extraction may also be carried out by 15 adding the solvent dropwise to a cylinder filled with the chopped raw or dried plant.

Plants of the genus Vitex L. in the family Verbenaceae

Examples of plants of the genus Vitex L. in the 20 family Verbenaceae usable in the present invention include simpleleaf chastetree (Vitex trifolia L.), roundleaf chastetree (Vitex rotundifolia L.f.), hempleaf negundo chastetree (Vitex cannabifolia Sieb. et Zucc.), negundo chastetree (Vitex negundo L.), and lilac chastetree (Vitex agnus-castus L.).

Preferable examples include lilac chastetree and simpleleaf chastetree.

In the present invention, plants of the genus Vitex L. in the family Verbenaceae can be used as ground 5 products of raw or dried plants, or as extracts obtained by effectively extracting active ingredients from the plants.

The part of the plants to be used is not limited, and the roots, trunks, branches, leaves, flowers, 10 fruit and other parts are usable.

Extracts of the plants can be obtained by chopping the raw or dried plant and then subjecting the chopped plant to extraction with a suitable solvent, which is preferably water, a lower alcohol or a mixture thereof.

15 Lower alcohols usable for extraction include C<sub>1-3</sub> alcohols, such as methanol, ethanol, etc., among which ethanol is most preferable. The alcohols may be hydrous alcohol (water content: 0.1 to 99.9%).

The extraction can be performed by a batch 20 process, percolation process, reflux process or other known processes. The amount of the extraction solvent is not limited, and is suitably 2 to 1000 parts relative to 1 part of the chopped raw or dried plant. The extraction can be carried out at room temperature or with heating.

25 Preferably, the extraction is performed at a

temperature range of room temperature to about 80°C for about 1 hour to about 10 hours while stirring under mild conditions. The extraction may be carried out by adding the solvent dropwise to a cylinder filled with the chopped 5 raw or dried plant.

Hair growth stimulant for oral use

The hair growth stimulant for oral use of the present invention comprises, as an active ingredient, at 10 least one member selected from the group consisting of plants of the genus Orthosiphon in the family Lamiaceae, plants of the genus Vitex L. in the family Verbenaceae, and extracts thereof.

The hair growth stimulant for oral use of the 15 present invention can be used as a preparation that is suitable as a health food, functional food, supplement or the like. The preparation can also be used as a medicine.

The hair growth stimulant for oral use of the present invention may consist solely of a plant or plants 20 of the genus Orthosiphon in the family Lamiaceae, a plant or plants of the genus Vitex L. in the family Verbenaceae and/or an extract or extracts thereof, or may be prepared by mixing the plant(s) and/or extract(s) with a material that is used as a carrier and then processing the mixture 25 into a powder, mass, liquid or other form.

Since plants of the genus Orthosiphon in the family Lamiaceae and the genus Vitex L. in the family Verbenaceae, and extracts thereof, show no toxicity for humans, the amount of the plant or plants and/or an extract or extracts thereof contained in the hair growth stimulant for oral use is not limited, and is preferably such that an adult human can orally ingest 0.1 to 100 g, and preferably 1 to 60 g (calculated as dried plant) of the plant or plants and/or extract or extracts thereof per day, divided into 1 to 3 doses.

The hair growth stimulant for oral use of the present invention may contain suitable additives as required.

The hair growth stimulant for oral use of the present invention can be formulated into an easily usable form, such as tablets, powder, granules, capsules, chewable tablets, liquid, etc.

Food

The hair growth stimulant for oral use of the present invention can be used in a so-called "food form", such as a food for hair growth.

The food comprising the hair growth stimulant for oral use of the present invention, such as a food for hair growth, can be prepared by processing the hair growth

stimulant for oral use alone, or by processing a mixture of the hair growth stimulant for oral use and an arbitrary material usable for food preparation, into a powder, mass, liquid or other form.

5           The food comprising the hair growth stimulant for oral use of the present invention used for a food can be made into various forms, such as a mass, liquid, syrup, powder, jelly, etc., in a routine manner.

10          Examples of food forms include soft drinks, juices, teas and other beverages (drink preparations); powdered juices, powdered soups and other powdered food; cookies, biscuits, cereals, chewing gums, candies, gummy candies, tablets, wafers, rice crackers and other confections and snacks; etc.

15          The food comprising the hair growth stimulant for oral use of the present invention may further contain other ingredients generally used in foods, to such an extent that the effects of the invention are not hindered. Examples of usable ingredients include other medicinal ingredients, nutrients, animal and plant ingredients, excipients, extenders, sweeteners, flavors, colors, preservatives, emulsifiers, solubilizers, polyhydric alcohols and ester derivatives thereof, organic and inorganic acids and salts thereof, water-soluble polymers, etc.

BEST MODE FOR CARRYING OUT THE INVENTION

The following Experiment and Examples are intended to illustrate the present invention in further 5 detail, and not to limit the scope thereof.

Experiment

(i) Preparation of extract

One hundred grams of a dried whole plant of 10 cat's whiskers, simpleleaf chastetree or lilac chastetree was chopped. Ethanol (2000 ml) was added, and the resulting mixture was heated to 70°C for 2 hours to perform extraction. After filtration, 2000 ml of ethanol was further added to the residue, and extraction was 15 carried out for 2 hours more. The filtrates obtained by the two extraction steps were combined, concentrated under reduced pressure, and freeze-dried to obtain an extract.

(ii) Test for hair regrowth promotion by external or oral 20 use, and evaluation of the test results

An area of about 2 x 4 cm was shaved on the back of nine 8-week-old C3H/He male mice (average weight: 25 g).

From the day following the day of shaving, 0.1 25 ml of a 50% aqueous ethanol solution containing 1 wt.% of

the extract obtained in (i) was applied to the shaved area of the group for testing external use, once a day for 10 days.

In the group for testing oral use, a 0.5% aqueous carboxymethylcellulose solution containing 5 wt.% of the extract obtained in (i) was orally administered in a dose containing 1 g of the extract per kg of body weight, once a day for 10 days.

Hair regrowth effect was evaluated by comparing the hair restoration in the shaved area. The average of the hair restoration results for the nine mice in each group was used for the comparison.

The hair regrowth promotion effect was expressed as a percentage relative to the hair restoration of the control group (external use of 50% ethanol or oral use of 0.5% carboxymethylcellulose), which was set to 100%, and the increment was presented as a hair regrowth promotion ratio. Table 1 shows the test results of the cat's whiskers extract.

Table 1

	Test substance	Hair restoration ratio (%)	Hair regrowth promotion ratio (%)
External use	Control	100	
	Cat's whiskers extract	121	21
Oral use	Control	100	
	Cat's whiskers extract	185	85

Table 1 reveals that the oral use of the cat's whiskers extract exhibits a higher hair regrowth promotion effect than the external use thereof. Similar results were obtained with respect to the simpleleaf chastetree extract and lilac chastetree extract.

Example 1: Formulation of sugar-coated tablets

The extracts prepared in the Experiment and other ingredients were mixed in the proportions shown in Examples 1-A to 1-C, and made into sugar-coated tablets in a routine manner.

Example 1-A

Ingredient	Proportion (%)
Dolomite (containing 20% of calcium and 10% of magnesium)	Balance
Powdered maltitol syrup	20

Lactose	17
Sucrose fatty acid ester	3
Cat's whiskers extract	5

5 Example 1-B

Ingredient	Proportion (%)
Dolomite (containing 20% of calcium and 10% of magnesium)	Balance
10 Powdered maltitol syrup	20
Lactose	17
Sucrose fatty acid ester	3
Lilac chastetree extract	5

15 Example 1-C

Ingredient	Proportion (%)
Dolomite (containing 20% of calcium and 10% of magnesium)	Balance
20 Powdered maltitol syrup	20
Lactose	17
Sucrose fatty acid ester	3
Simpleleaf chastetree extract	5

25 Example 2: Formulation of tablets

The extracts prepared in the Experiment and other ingredients were mixed in the proportions shown in

Examples 2-A to 2-C, and made into tablets in a routine manner.

**Example 2-A**

	<b>Ingredient</b>	<b>Proportion (%)</b>
5	Dextrin	Balance
	Powdered maltitol syrup	20
	Lactose	20
	Trehalose	10
10	Cat's whiskers extract	5
	Aspartame	Trace
	Flavor	Trace

**Example 2-B**

	<b>Ingredient</b>	<b>Proportion (%)</b>
15	Dextrin	Balance
	Powdered maltitol syrup	20
	Lactose	20
	Trehalose	10
20	Lilac chastetree extract	5
	Aspartame	Trace
	Flavor	Trace

**Example 2-C**

	<b>Ingredient</b>	<b>Amount (%)</b>
--	-------------------	-------------------

Dextrin	Balance
Powdered maltitol syrup	20
Lactose	20
Trehalose	10
5 Simpleleaf chastetree extract	5
Aspartame	Trace
Flavor	Trace

Example 3: Formulation of drink preparation

10 The extracts prepared in the Experiment and other ingredients were mixed in the proportions shown in Examples 3-A to 3-C, and made into drink preparations in a routine manner.

15 Example 3-A

Ingredient	Amount (%)
Cat's whiskers extract	5
Sucrose	2
Ascorbic acid	1.5
20 Preservative	Trace
Flavor	Trace
Purified Water	Balance

Example 3-B

25 Ingredient Proportion (%)

Lilac chastetree extract	5
Sucrose	2
Ascorbic acid	1.5
Preservative	Trace
5 Flavor	Trace
Purified water	Balance

Example 3-C

Ingredient	Amount (%)
Simpleleaf chastetree extract	5
Sucrose	2
Ascorbic acid	1.5
Preservative	Trace
Flavor	Trace
15 Purified water	Balance

INDUSTRIAL APPLICABILITY

The hair growth stimulant for oral use of the present invention, i.e., a hair growth stimulant for oral use comprising at least one member selected from the group consisting of plants of the genus Orthosiphon in the family Lamiaceae, plants of the genus Vitex L. in the family Verbenaceae, and extracts thereof, has an excellent hair growth activity and exhibits excellent effects of hair loss prevention, hair regrowth promotion, etc.

Further, the food comprising the hair growth stimulant shows excellent effects of hair loss prevention, hair regrowth promotion, etc., and are useful as foods for hair regrowth and like purposes.